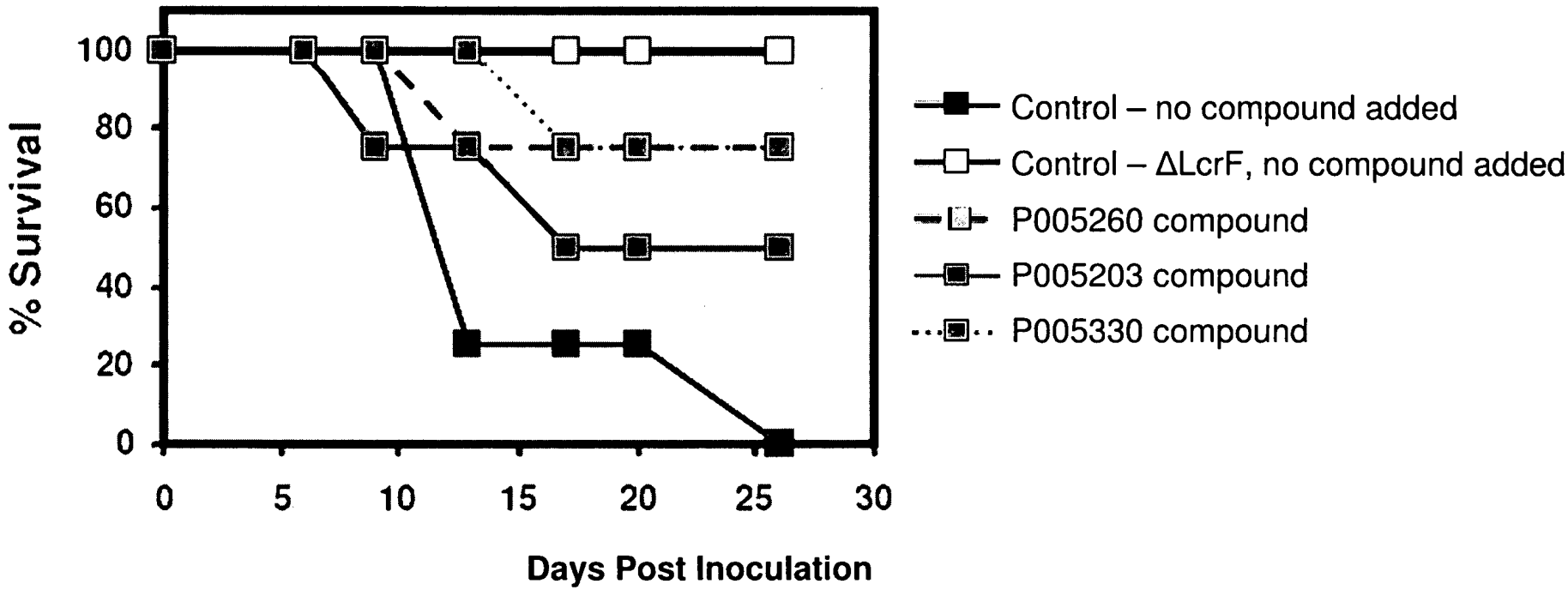
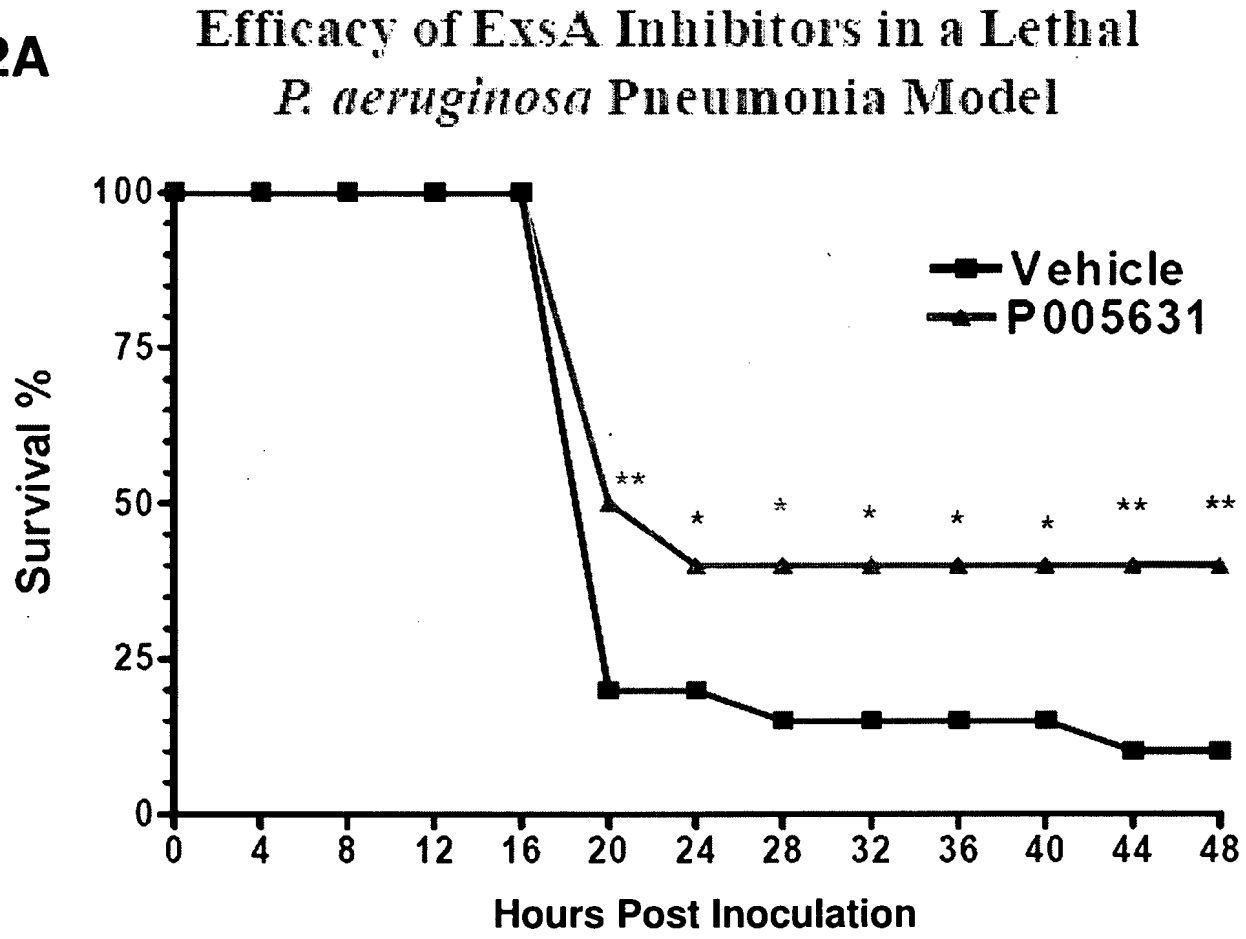
Figure 1

Efficacy of LcrF Inhibitors in a Lethal *Y. pseudotuberculosis* Pneumonia Model



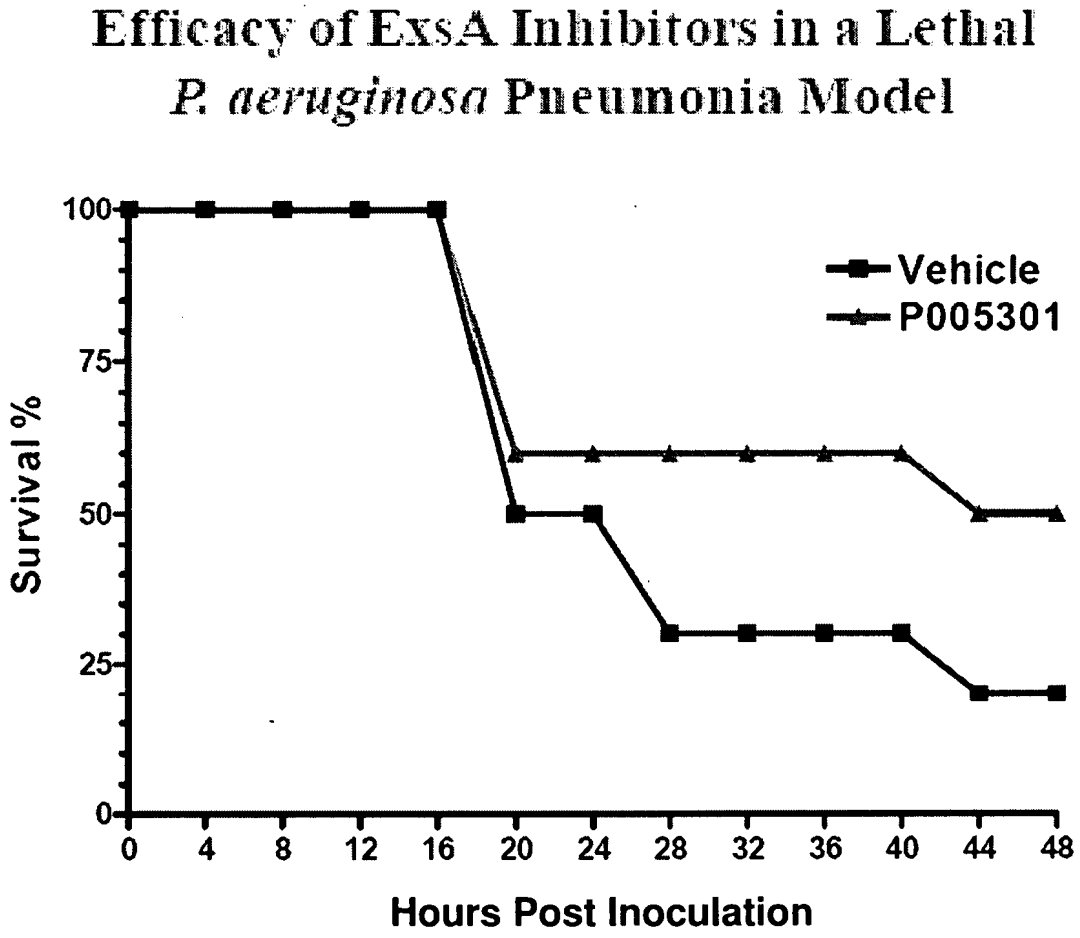
Groups of 4 CD1 mice (7-8 week old males) were dosed subcutaneously with either vehicle or compound (25 mg/kg) 1 day prior to inoculation, at the time of inoculation (0h), at 8h, and then daily for 8 days following intranasal inoculation with ~120 CFU of wild type (WT, IP2666pIB1) or ΔLcrF (JMB155) *Y. pseudotuberculosis*. Note that % Survival data for P005260 and P005330 run on top of each other.

Figure 2A



Efficacy of P005631 and P005301, prototypic ExsA inhibitors, vs. *Pseudomonas aeruginosa* PA103 in a mouse lethal pneumonia model (10^6 organisms inoculated intranasally). P005631 was administered IP at 25 mg/kg at 18 hours before inoculation, 1 hour before inoculation and 2, 5, 20, 26, and 44 hours inoculation. Mortality was assessed at various times post inoculation. A statistically significant difference was noted between the untreated (vehicle) and the P005631 treated groups.
** $p<0.05$, * $p<0.1$ by Chi-Square analysis, n = 22 mice/group.

Figure 2B



P005301 was administered IP at 25 mg/kg at 18 hours before inoculation, 1 hour before inoculation and 5, 20, 26, and 44 hours post-inoculation. Mortality was assessed at various times post inoculation, n = 6-8 mice/group.

Figure 3

Efficacy of LcrF Inhibitors in a Non-Lethal Lung Infection Model

LcrF inhibitors that exhibited activity in the cell free DNA binding assay and *Y. pseudotuberculosis* cytotoxicity assay were tested for *in vivo* efficacy using a non-lethal lung infection model.

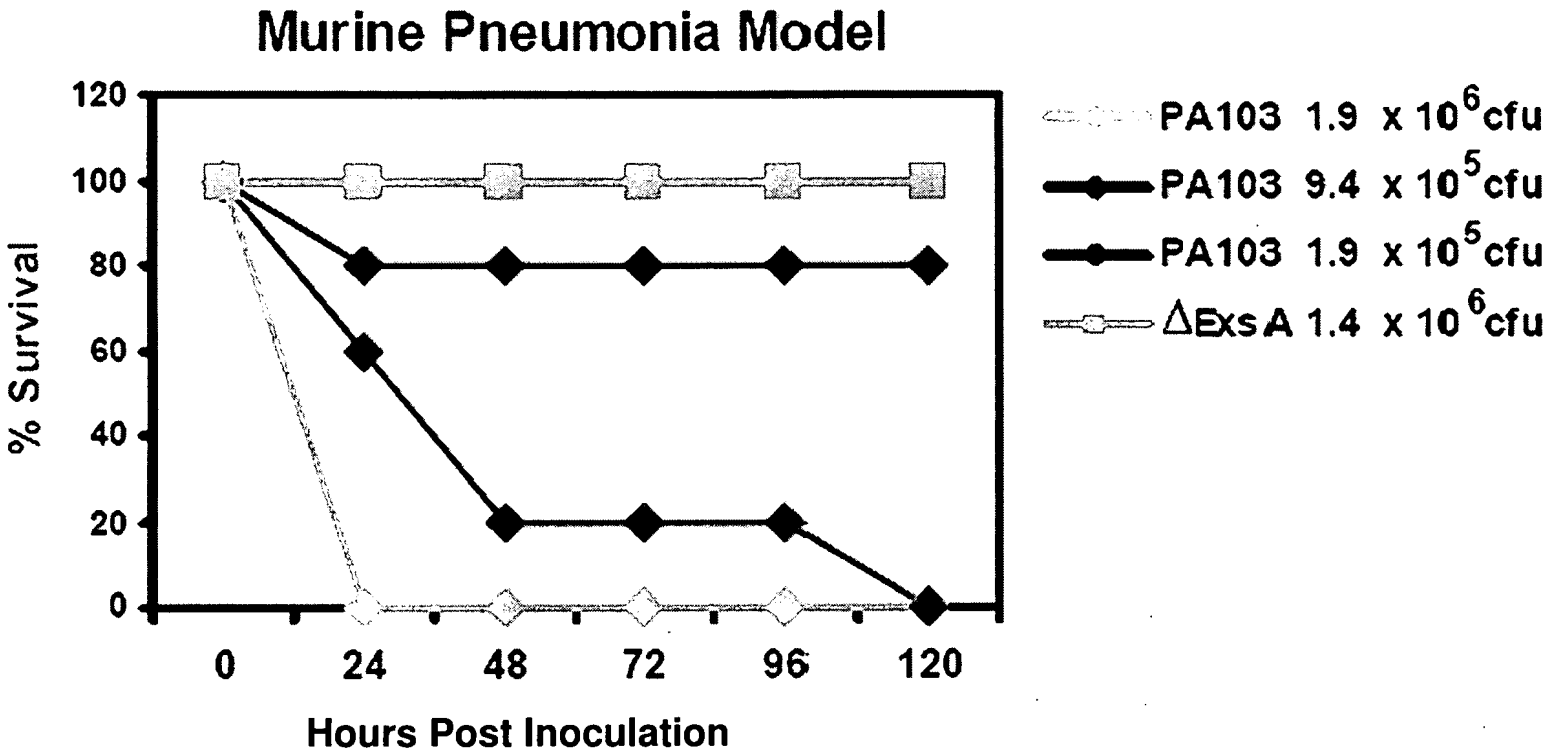
Groups of 4 CD-1 mice (7-8 week old males) were treated with a single subcutaneous dose of vehicle or LcrF inhibitor (25 mg/kg) 1 day prior to infection, at the time of infection, at 8 h post infection, then once daily for a further 2 days. Mice were inoculated intranasally with ~700 CFU of WT (IP2666pIB1) or ΔLcrF (JMB155) *Y. pseudotuberculosis*. Mice were sacrificed 3 days post inoculation and serial dilutions of lung tissue homogenates were plated.

Compound	Log Decrease in CFU/g Lung Tissue[a]
P005203	1.5
P005330	0.8
P005260	1.1
ΔLcrF, no compound added	2.0

[a] Decrease relative to vehicle treated mice infected with wild type *Y. pseudotuberculosis*.

Figure 4

ExsA Mutants are Avirulent in Animal Models of Infection



Murine Pneumonia Model: Groups of 5 Swiss Webster mice were inoculated intranasally with the indicated numbers of bacteria in 50µL PBS.